

Current Claims of the Bova Application

1. A method of treating hyperlipidemia in a hyperlipidemic comprising dosing the hyperlipidemic with an effective antihyperlipidemic amount of nicotinic acid once per day in the evening or at night, wherein said nicotinic acid is combined with at least one pharmaceutically acceptable carrier to form an oral solid dosage form.
2. A method, as set forth in Claim 1, wherein the hyperlipidemic is dosed with from about 250 milligrams to about 3000 milligrams of nicotinic acid.
3. A method as set forth in Claim 1 which causes little or no serious liver damage.
4. A method as set forth in Claim 1 wherein the release rate of said nicotinic acid is from about 2.0% per hour to about 25% per hour.
5. A method as set forth in Claim 6 wherein said nicotinic acid is prepared by formulating the active compound with from about 5 to about 50 parts by weight of hydroxypropyl methylcellulose per 100 parts by weight of tablet.
6. A method, as set forth in Claim 1, wherein said nicotinic acid is dosed in the form of a sustained release tablet containing from about 1 to about 4 parts by weight of binder per 100 parts by weight of tablet.
7. A method, as set forth in Claim 6, wherein said binder is polyvinyl pyrrolidone.

8. A method, as set forth in Claim 1, wherein said nicotinic acid is dosed in the form of a sustained release tablet comprising from about 0.5 to about 2.5 parts by weight of a lubricating agent per 100 parts by weight of tablet.

9. A method, as set forth in Claim 8, wherein said lubricating agent is selected from the group consisting of stearic acid and magnesium stearate.

13. A method of treating hyperlipidemia in a hyperlipidemic comprising dosing the hyperlipidemic with an effective antihyperlipidemic amount of a compound metabolized to nicotinic acid by the body and selected from the group consisting of nicotinyl alcohol tartrate, d-glucitol hexanicotinate, aluminum nicotinate, and, 1-alpha-tocopheryl nicotinate, once per day in the evening or at night combined with at least one pharmaceutically acceptable carrier, to produce a reduction in total and LDL cholesterol, triglycerides and Lp(a), with a significant increase in HDL cholesterol.

14. A method of treating hyperlipidemia in a hyperlipidemic comprising dosing the hyperlipidemic with an effective antihyperlipidemic amount of a compound metabolized to nicotinic acid by the body and selected from the group consisting of nicotinyl alcohol tartrate, d-glucitol hexanicotinate, aluminum nicotinate, and, 1-alpha-tocopheryl nicotinate, once per day in the evening or at night combined with at least one pharmaceutically acceptable carrier.

15. A method of treating hyperlipidemia in a hyperlipidemic comprising the administration of an effective antihyperlipidemic amount of a nicotinic acid composition once per day in the evening or at night, wherein said nicotinic acid composition is an oral solid dosage form that consists essentially of nicotinic acid, hydroxypropyl methylcellulose, a binder and a lubricant.

ATTACHMENT B

Attorney Docket No. 32892.32

PATENT

**Submitted under:
37 C.F.R. §1.102; and
M.P.E.P. §708.2 (XII)
Petition to Make Special**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: David J. Bova
Serial No.: 08/814,974
Filing Date: March 6, 1997
Group Art Unit: 1931
Examiners: Richard Schwartz, Biotechnology Practice Specialist
J. Venkat
Title: METHODS AND SUSTAINED RELEASED NICOTINIC ACID
COMPOSITIONS FOR TREATING HYPERLIPIDEMIA AT
NIGHT

Assistant Commissioner of Patents
Washington, D.C. 20231

Pending Claims 22-~~194~~² in Amendment after October 28th Interview

Group I - claims 22-145

(22) A daily method of treating hyperlipidemia in a patient without inducing treatment-limiting liver damage, said daily method comprising orally dosing the patient with an effective antihyperlipidemic amount of nicotinic acid once per day during the evening or at night as a single dose, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable carrier to form an oral sustained release solid dosage form, and wherein the oral sustained release solid

dosage form does not contain an internal hydrophobic component, said single daily dose treatment causing little or no serious damage to the liver of the patient.

(23) A method, as set forth in claim 22, wherein the patient is dosed with from about 250 mg to about 3000 mg of nicotinic acid.

(24) A method, as set forth in claim 23, wherein the release rate of the nicotinic acid is from about 2.0% per hour to about 25% per hour.

(25) A method, as set forth in claim 22, wherein the oral sustained release solid dosage form is prepared by formulating the nicotinic acid with from about 5 parts to about 50 parts by weight of hydroxypropyl methylcellulose per 100 parts by weight of the oral sustained release solid dosage form.

(26) A method, as set forth in claim 22, wherein the oral sustained release solid dosage form contains from about 1 part to about 4 parts by weight of binder per 100 parts by weight of the oral sustained release solid dosage form.

(27) A method, as set forth in claim 24, wherein the binder is a polymer having the repeating polymerization unit 1-ethenyl-2-pyrrolidone.

(28) A method, as set forth in claim 22, wherein the oral sustained release solid dosage form contains from about 0.5 parts to about 2.5 parts by weight of a lubricant per 100 parts by weight of the oral sustained release solid dosage form.

(29) A method, as set forth in claim 28, wherein the lubricant is selected from the group consisting of lubricants consisting of stearic acid and magnesium stearate.

(30) A method, as set forth in claim 22, wherein the oral sustained release solid dosage form contains from about 250 mg to about 3000 mg of nicotinic acid.

(31) A method, as set forth in claim 22, wherein the oral sustained release solid dosage form is an oral sustained release tablet.

(32) A method, as set forth in claim 31, wherein the oral sustained release tablet contains nicotinic acid in an amount selected from the group consisting of about 375 mg, about 500 mg and about 750 mg.

(33) A method, as set forth in claim 31, wherein the oral sustained release tablet contains

- (a) about 375 mg nicotinic acid,
- (b) about 189 mg hydroxypropyl methylcellulose as a swelling agent
- (c) about 13 mg a polymer having the repeating polymerization unit 1-ethenyl-2-pyrrolidone as a binder, and
- (d) about 6 mg of stearic as a lubricant.

(34) A method, as set forth in claim 31, wherein the oral sustained release tablet contains

- (a) about 500 mg nicotinic acid,
- (b) about 203 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 17.2 mg polyvinyl pyrrolidone as a binder, and
- (d) about 7.3 mg stearic acid as a lubricant.

(35) A method, as set forth in claim 31, wherein the oral sustained release tablet contains

- (a) about 750 mg nicotinic acid,
- (b) about 205 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 26 mg polyvinyl pyrrolidone as a binder, and
- (d) about 10 mg stearic acid as a lubricant.

(36) A method, as set forth in claim 31, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% by weight nicotinic acid,
- (b) about 5% to about 50% by weight hydroxypropyl methylcellulose as a swelling agent,

- (c) about 1% to about 5% by weight a polymer having repeating polymerization unit 1-ethenyl-2-pyrrolidone as a binder, and
- (d) about 0.5% to about 2% by weight stearic acid as a lubricant.

(37) A method, as set forth in claim 31, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% parts by weight nicotinic acid, and
- (b) about 5% to about 50% parts by weight hydroxypropyl methylcellulose as a swelling agent.

(38) A method, as set forth in claim 22, wherein said single dose treatment during the evening or at night elevates HDL cholesterol in the patient.

(39) A method, as set forth in claim 22, wherein said single dose treatment during the evening or at night results in little or no serious increase in a liver function test in the patient, wherein the liver function test is selected from the group consisting of an AST, ALT and alkaline phosphatase liver function test.

(40) A method, as set forth in claim 22, wherein said single dose treatment during the evening or at night results in little or no serious increase in uric acid in the patient.

(41) A method, as set forth in claim 22, wherein said single dose treatment during the evening or at night results in little or no serious increase in free fasting glucose in the patient.

(42) A composition for treating hyperlipidemia in a patient with an effective amount of nicotinic acid once per day during the evening or at night, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form an oral sustained release solid dosage form, and wherein said oral sustained release solid dosage form does not contain an internal hydrophobic component.

(43) A composition, as set forth in claim 42, wherein said oral solid dosage form comprises from about 250 mg to about 3000 mg of nicotinic acid.

(44) A composition, as set forth in claim 42, wherein the release rate of said nicotinic acid is from about 2.0% per hour to about 25% per hour.

(45) A composition, as set forth in claim 42, wherein said oral solid dosage form is comprises from about 5 to about 50 parts by weight of hydroxypropyl methylcellulose per 100 parts by weight of the oral solid dosage form.

(46) A composition, as set forth in claim 42, wherein said oral solid dosage form further contains from about 1 to about 4 parts by weight of a binder per 100 parts by weight of the oral solid dosage form.

(47) A composition, as set forth in claim 46, wherein said binder is polyvinyl pyrrolidone.

(48) A composition, as set forth in claim 42, wherein said oral solid dosage form further contains from about 0.5 to about 2.5 parts by weight of a lubricant per 100 parts by eight of the solid dosage form.

(49) A composition, as set forth in claim 48, wherein said lubricant is selected from the group consisting of stearic acid and magnesium stearate.

(50) A composition, as set forth in claim 42, wherein said oral sustained release solid dosage form is an oral sustained release tablet comprising from about 250 mg to about 3000 mg of nicotinic acid.

(51) A composition, as set forth in claim 42, wherein said oral sustained release solid dosage form is an oral sustained release tablet.

(52) A composition, as set forth in claim 51, wherein said oral sustained released tablet contains nicotinic acid in an amount selected from the group consisting of about 375 mg, about 500 mg and about 750 mg.

(53) A composition, as set forth in claim 51, wherein said oral sustained release tablet contains

- (a) about 375 mg nicotinic acid,
- (b) about 189 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 13 mg polyvinyl pyrrolidone as a binder, and
- (d) about 6 mg of stearic acid as a lubricant.

(54) A composition, as set forth in claim 51, wherein said oral sustained release tablet contains

- (a) about 500 mg nicotinic acid,
- (b) about 203 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 17 mg polyvinyl pyrrolidone as a binder, and
- (d) about 7 mg stearic acid as a lubricant.

(55) A composition, as set forth in claim 51, wherein said oral sustained release tablet contains

- (a) about 750 mg nicotinic acid,
- (b) about 205 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 26 mg polyvinyl pyrrolidone as a binder, and
- (d) about 10 mg stearic acid as a lubricant.

(56) A composition, as set forth in claim 51, wherein said oral sustained release tablet contains

- (a) about 30% to about 90% by weight nicotinic acid,
- (b) about 5% to about 50% by weight hydroxypropyl methylcellulose as a swelling agent,
- (c) about 1% to about 5% by weight polyvinyl pyrrolidone as a binder, and
- (d) about 0.5% to about 2% by weight stearic acid as a lubricant.

(57) A composition, as set forth in claim 51, wherein said oral sustained release tablet contains

- (a) about 30% to about 90% parts by weight nicotinic acid, and

(b) about 5% to about 50% parts by weight hydroxypropyl methylcellulose as a swelling agent.

(58) A composition, as set forth in claim 42, wherein said oral sustained release solid dosage form elevates HDL cholesterol in the patient.

(59) A composition, as set forth in claim 42, said oral sustained release solid dosage form causing little or no serious increase in a liver function test in the patient when said oral sustained release solid dosage form is taken during the evening or at night as a single dose, wherein the liver function test is selected from the group consisting of an AST, ALT and alkaline phosphatase liver function test.

(60) A method, as set forth in claim 42, said oral sustained release solid dosage form causes little or no serious increase in uric acid in the patient when said oral sustained release solid dosage form is taken during the evening or at night as a single dose.

(61) A method, as set forth in claim 42, oral sustained release solid dosage form causes little or no serious increase in free fasting glucose in the patient when said oral sustained release solid dosage form is taken during the evening or at night as a single dose.

(62) A composition for treating hyperlipidemia in a patient with an effective amount of nicotinic acid once per day during the evening or at night as a single dose for a lowering serum lipid without inducing treatment-limiting liver damage, wherein the serum lipid is selected from the group consisting of total cholesterol, LDL cholesterol, triglycerides and Lp(a), and wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form an oral sustained release solid dosage form, and wherein said oral sustained release solid dosage form does not contain an internal hydrophobic component.

(63) A composition, as set forth in claim 62, wherein said oral sustained release solid dosage form comprises from about 250 mg to about 3000 mg of nicotinic acid.

(64) A composition, as set forth in claim 62, wherein the release rate of said nicotinic acid is from about 2.0% per hour to about 25% pr hour.

(65) A composition, as set forth in claim 62, wherein said oral sustained release solid dosage form elevates HDL cholesterol in the patient.

(66) A composition, as set forth in claim 61, wherein said oral sustained release solid dosage form is an oral sustained release tablet.

(67) A composition , as set forth in claim 62, said oral sustained release solid dosage form causes little or no serious increase in uric acid in the patient when said oral sustained release solid dosage form is taken during the evening or at night as a single dose.

(68) A composition, as set forth in claim 62, said oral sustained release solid dosage form causes little or no serious increase in free fasting glucose in the patient when said oral sustained release solid dosage form is taken during the evening or at night as a single dose.

(69) A composition, as set forth in claim 62, wherein said oral sustained release solid dosage form contains about 5 to about 50 parts by weight of hydroxypropyl methylcellulose per 100 parts by weight of the oral sustained release solid dosage form as the swelling agent.

(70) A composition, as set forth in claim 62, wherein said oral sustained release solid dosage form further contains from about 1 to about 4 parts by weight of a binder per 100 parts by weight of the oral sustained release solid dosage form.

(71) A composition, as set forth in claim 70, wherein the binder is polyvinyl pyrrolidone.

(72) A composition, as set forth in claim 62, wherein said oral sustained release solid dosage form further contains from about 0.5 to about 2.5 parts by weight of a lubricant per 100 parts by weight of the oral sustained release solid dosage form.

(73) A composition, as set forth in claim 72, wherein said lubricant is selected from the group consisting of stearic acid and magnesium stearate.

(74) A composition, as set forth in claim 62, wherein said oral sustained release solid dosage form contains from about 250 mg to about 3000 mg of nicotinic acid.

(75) A composition, as set forth in claim 62, wherein said sustained release solid dosage form contains

- (a) about 30% to about 90% parts by weight nicotinic acid,
- (b) about 5% to about 50% parts by weight hydroxypropyl methylcellulose as the swelling agent.

(76) A composition, as set forth in claim 62, wherein said oral sustained release solid dosage form contains

- (a) about 30% to about 90% by weight nicotinic acid,
- (b) about 5% to about 50% by weight hydroxypropyl methylcellulose as a swelling agent,
- (c) about 1% to about 5% by weight a polymer having repeating polymerization unit 1-ethenyl-2-pyrrolidone as a binder, and
- (d) about 0.5% to about 2% by weight stearic acid as a lubricant.

(77) A composition, as set forth in claim 62, wherein said [the] sustained release solid dosage form contains

- (a) about 375 mg nicotinic acid,
- (b) about 189 mg hydroxypropyl methylcellulose as the swelling agent,
- (c) about 13 mg polyvinyl pyrrolidone as the binder, and
- (d) about 6 mg of stearic acid as the lubricant.

(78) A method, as set forth in claim 62, wherein said sustained release solid dosage form contains

- (a) about 500 mg nicotinic acid,
- (b) about 203 mg hydroxypropyl methylcellulose as the swelling agent,

- (c) about 17 mg polyvinyl pyrrolidone as the binder, and
- (d) about 7 mg stearic acid as the lubricant.

(79) A method, as set forth in claim 62, wherein said sustained release solid dosage form contains

- (a) about 750 mg nicotinic acid,
- (b) about 205 mg hydroxypropyl methylcellulose as the swelling agent,
- (c) about 26 mg polyvinyl pyrrolidone as the binder, and
- (d) about 10 mg stearic acid as the lubricant.

(80) A method of treating hyperlipidemia in a patient without inducing treatment-limiting (i) hepatotoxicity and (ii) abnormalities in uric acid levels or glucose levels or both, said method comprising orally dosing the patient with an effective antihyperlipidemic amount of nicotinic acid once per day during the evening or at night as a single dose, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form an oral sustained release solid dosage form, and wherein the oral sustained release solid dosage form does not contain an internal hydrophobic component, and wherein the oral sustained release solid dosage form is effective in reducing a serum lipid without causing treatment-limiting (i) hepatotoxicity and (ii) elevations in uric acid levels or glucose levels or both in the patient to a level which would require said treatment to be discontinued by the patient when it is ingested by the patient once per day during the evening or at night as the single dose in accordance with said single dose treatment.

(81) A composition of nicotinic acid for oral administration to a patient once per day during the evening or at night as the patient lies down to go to sleep for providing an effective antihyperlipidemic amount of nicotinic acid to the patient during times of peak lipid production or synthesis by the patient to induce at least some lowering of total cholesterol, LDL cholesterol, triglycerides and Lp(a) and at least some increase in HDL cholesterol in the patient's blood stream, without causing abnormalities in uric acid levels or glucose levels or both to an extent which would require said daily treatment to be discontinued by the patient, the sustained release composition comprising an effective antihyperlipidemic amount of nicotinic acid and an excipient to provide

sustained release of the nicotinic acid, and wherein the sustained release solid dosage form does not contain an internal hydrophobic component.

- (82) A composition of claim 81, wherein the effective antihyperlipidemic amount of nicotinic acid is from about 250 mg to about 3000 mg of nicotinic acid.
- (83) A composition of claim 81, wherein said excipient is selected from the group consisting of a swelling agent, a binder, a processing aid and mixtures thereof.
- (84) A composition of claim 83, wherein said swelling agent is selected from group consisting of a polymer, a wax, a natural material and mixtures thereof.
- (85) A composition of claim 84, wherein said polymer is selected from the group consisting of hydroxypropyl methylcellulose, sodium carboxymethylcellulose and ethylcellulose.
- (86) A composition of claim 84, wherein said wax is bees wax.
- (87) A composition of claim 84, wherein said natural material is selected from the group consisting of gums and gelatins.
- (88) A composition of claim 83, wherein said binder is povidone.
- (89) A composition of claim 83, wherein said processing aid is a lubricant.
- (90) A composition of claim 89, wherein said lubricant is stearic acid.
- (91) A composition of claim 85, wherein said hydroxypropyl methylcellulose is in an amount ranging from about 5% to about 50% parts by weight per 100 parts by weight of said sustained release composition.

(92) A composition of claim 83, wherein said binder is in an amount ranging from about 1% to about 5% parts by weight per 100 parts by weight of said sustained release composition.

(93) A composition of claim 83, wherein said processing aid is in an amount ranging from about 0.5% to about 2% parts by weight per 100 parts by weight of said sustained release composition.

(94) A composition of claim 81, wherein said sustained release composition consists essentially of nicotinic acid, hydroxypropyl methylcellulose, povidone and stearic acid.

(95) A composition of claim 81, wherein said sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 375.0 mg, |
| hydroxypropyl methylcellulose | 188.7 mg, |
| povidone | 12.9 mg, and |
| stearic acid | 5.8 mg. |

(96) A composition of claim 81, wherein said sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 500.0 mg, |
| hydroxypropyl methylcellulose | 203.0 mg, |
| povidone | 17.2 mg, and |
| stearic acid | 7.3 mg. |

(97) A composition of claim 81, wherein said sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 750.0 mg, |
| hydroxypropyl methylcellulose | 204.7 mg, |
| povidone | 25.9 mg, and |
| stearic acid | 9.9 mg. |

(98) A sustained release composition of nicotinic acid for oral administration to a patient once per day during the evening or at night or as the patient lies down to go to sleep for providing an effective antihyperlipidemic amount of nicotinic acid to the patient during times of peak lipid production or synthesis by the patient to induce at least some lowering of total cholesterol, LDL cholesterol, triglycerides and Lp(a) and at least some increase in HDL cholesterol in the patient's blood stream, without causing abnormalities in uric acid levels or glucose levels or both to an extent which would require the use of said sustained release composition by the patient to be discontinued, said sustained release composition comprising (a) an effective antihyperlipidemic amount of nicotinic acid, and (b) an excipient to provide sustained release of the nicotinic acid.

(99) A sustained release composition of claim 98, wherein said excipient is selected from the group consisting of a swelling agent, a binder, a processing aid and mixtures thereof.

(100) A sustained release composition of claim 99, wherein said swelling agent is selected from group consisting of a polymer, a wax, a natural material and mixtures thereof.

(101) A sustained release composition of claim 100, wherein said polymer is selected from the group consisting of hydroxypropyl methylcellulose, sodium carboxymethylcellulose and ethylcellulose.

(102) A sustained release composition of claim 100, wherein said wax is bees wax.

(103) A sustained release composition of claim 100, wherein said natural material is selected from the group consisting of gums and gelatins.

(104) A sustained release composition of claim 99, wherein said binder is povidone.

(105) A sustained release composition of claim 99, wherein said processing aid is a lubricant.

(106) A sustained release composition of claim 105, wherein said lubricant is stearic acid.

(107) A sustained release composition of claim 101, wherein said hydroxypropyl methylcellulose is in an amount ranging from about 5% to about 50% parts by weight per 100 parts by weight of said sustained release composition.

(108) A sustained release composition of claim 99, wherein said binder is in an amount ranging from about 1% to about 5% parts by weight per 100 parts by weight of said sustained release composition.

(109) A sustained release composition of claim 99, wherein said processing aid is in an amount ranging from about 0.5% to about 2% parts by weight per 100 parts by weight of said sustained release composition.

(110) A sustained release composition of claim 98, wherein said sustained release composition consists essentially of nicotinic acid, hydroxypropyl methylcellulose, povidone and stearic acid.

(111) A sustained release composition of claim 98, wherein said sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 375.0 mg, |
| hydroxypropyl methylcellulose | 188.7 mg, |
| povidone | 12.9 mg, and |
| stearic acid | 5.8 mg. |

(112) A sustained release composition of claim 98, wherein said sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 500.0 mg, |
| hydroxypropyl methylcellulose | 203.0 mg, |
| povidone | 17.2 mg, and |
| stearic acid | 7.3 mg. |

(113) A sustained release composition of claim 98, wherein said sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 750.0 mg, |
| hydroxypropyl methylcellulose | 204.7 mg, |
| povidone | 25.9 mg, and |
| stearic acid | 9.9 mg. |

(114) A daily method of treating hyperlipidemia in a patient without inducing treatment-limiting elevations in uric acid levels or glucose levels or both in the patient, said daily method comprising orally dosing the patient with an effective antihyperlipidemic amount of nicotinic acid once per day during the evening or at night as a single dose, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable carrier to form an oral sustained release solid dosage form, and wherein the oral sustained release solid dosage form does not contain an internal hydrophobic component.

(115) A method, as set forth in claim 114, wherein the patient is dosed with from about 250 mg to about 3000 mg of nicotinic acid.

(116) A method, as set forth in claim 115, wherein the release rate of the nicotinic acid is from about 2.0% per hour to about 25% per hour.

(117) A method, as set forth in claim 114, wherein the oral sustained release solid dosage form is prepared by formulating the nicotinic acid with from about 5 parts to about 50 parts by weight of hydroxypropyl methylcellulose per 100 parts by weight of the oral sustained release solid dosage form.

(118) A method, as set forth in claim 114, wherein the oral sustained release solid dosage form contains from about 1 part to about 4 parts by weight of binder per 100 parts by weight of the oral sustained release solid dosage form.

(119) A method, as set forth in claim 116, wherein the binder is a polymer having the repeating polymerization unit 1-ethenyl-2-pyrrolidone.

(120) A method, as set forth in claim 114, wherein the oral sustained release solid dosage form contains from about 0.5 parts to about 2.5 parts by weight of a lubricant per 100 parts by weight of the oral sustained release solid dosage form.

(121) A method, as set forth in claim 120, wherein the lubricant is selected from the group consisting of lubricants consisting of stearic acid and magnesium stearate.

(122) A method, as set forth in claim 114, wherein the oral sustained release solid dosage form contains from about 250 mg to about 3000 mg of nicotinic acid.

(123) A method, as set forth in claim 114, wherein the oral sustained release solid dosage form is an oral sustained release tablet.

(124) A method, as set forth in claim 123, wherein the oral sustained release tablet contains nicotinic acid in an amount selected from the group consisting of about 375 mg, about 500 mg and about 750 mg.

(125) A method, as set forth in claim 123, wherein the oral sustained release tablet contains

- (a) about 375 mg nicotinic acid,
- (b) about 189 mg hydroxypropyl methylcellulose as a swelling agent
- (c) about 13 mg a polymer having the repeating polymerization unit 1-ethenyl-2-pyrrolidone as a binder, and
- (d) about 6 mg of stearic as a lubricant.

(126) A method, as set forth in claim 123, wherein the oral sustained release tablet contains

- (a) about 500 mg nicotinic acid,
- (b) about 203 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 17.2 mg polyvinyl pyrrolidone as a binder, and

- (d) about 7.3 mg stearic acid as a lubricant.

(127) A method, as set forth in claim 123, wherein the oral sustained release tablet contains

- (a) about 750 mg nicotinic acid,
- (b) about 205 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 26 mg polyvinyl pyrrolidone as a binder, and
- (d) about 10 mg stearic acid as a lubricant.

(128) A method, as set forth in claim 123, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% by weight nicotinic acid,
- (b) about 5% to about 50% by weight hydroxypropyl methylcellulose as a swelling agent,
- (c) about 1% to about 5% by weight a polymer having repeating polymerization unit 1-ethenyl-2-pyrrolidone as a binder, and
- (d) about 0.5% to about 2% by weight stearic acid as a lubricant.

(129) A method, as set forth in claim 123, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% parts by weight nicotinic acid, and
- (b) about 5% to about 50% parts by weight hydroxypropyl methylcellulose as a swelling agent.

(130) A method, as set forth in claim 114, wherein said single dose treatment during the evening or at night elevates HDL cholesterol in the patient.

(131) A daily method of treating hyperlipidemia in a patient without inducing treatment-limiting abnormalities in uric acid levels or glucose levels or both in the patient, said daily method comprising orally dosing the patient with an effective antihyperlipidemic amount of nicotinic acid once per day during the evening or at night or as the patient lies down to go to sleep as a single dose for providing an effective antihyperlipidemic amount of nicotinic acid to the patient during times of peak lipid production or synthesis by the patient to induce at least some decrease in levels of total cholesterol, LDL cholesterol, triglycerides and Lp(a) in the patient and to induce at least some increase in levels of HDL cholesterol in the patient, without causing abnormalities in either uric acid

or glucose levels or both to an extent which would require said daily treatment to be discontinued by the patient, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form an oral sustained release solid dosage form, and wherein said oral sustained release solid dosage form does not contain an internal hydrophobic component.

(132) A method, as set forth in claim 131, wherein said single dose treatment induces at least some decrease in levels of total cholesterol, LDL cholesterol, triglycerides and Lp(a) in the patient.

(133) A method, as set forth in claim 131, wherein said single dose treatment elevates HDL cholesterol in the patient.

(134) A method of treating hyperlipidemia in a human without causing treatment-limiting hepatotoxicity or elevations in uric acid levels or glucose levels or both in the human, said daily treatment comprising ingesting orally an effective anti-hyperlipidemic amount of nicotinic acid once per day as a single dose for providing an effective antihyperlipidemic amount of nicotinic acid to the human during times of peak lipid production or synthesis by the human without causing treatment-limiting elevations in uric acid or glucose levels or both in the human, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form an oral sustained release solid dosage form, and wherein the oral sustained release solid dosage form does not contain an internal hydrophobic component.

(135) A method, as set forth in claim 134, wherein said single dose treatment induces at least some decrease in levels of total cholesterol, LDL cholesterol, triglycerides and Lp(a) in the human.

(136) A method, as set forth in claim 134, wherein said single dose treatment elevates HDL cholesterol in the human.

(137) A method of treating hyperlipidemia in a hyperlipidemic comprising dosing the hyperlipidemic with an effective antihyperlipidemic amount of nicotinic acid once per day in the

evening or at night, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable carrier to form an oral solid dosage form, and wherein the oral solid dosage form does not contain an internal hydrophobic component.

(138) A method, as set forth in claim 137, wherein the hyperlipidemic is dosed with from about 250 milligrams to about 3000 milligrams of nicotinic acid.

(139) A method, as set forth in claim 137, which causes little or no serious liver damage.

(140) A method, as set forth in claim 137, wherein the release rate of said nicotinic acid is from about 2.0% per hour to about 25% per hour.

(141) A method, as set forth in claim 137, wherein said nicotinic acid is prepared by formulating the active compound with from about 5 parts to about 50 parts by weight of hydroxypropyl methylcellulose per 100 parts by weight of tablet.

(142) A method, as set forth in claim 137, wherein said nicotinic acid is dosed in the form of a sustained release tablet containing from about 1 part to about 4 parts by weight of binder per 100 parts by weight of tablet.

(143) A method, as set forth in claim 142, wherein said binder is polyvinyl pyrrolidone.

(144) A method, as set forth in claim 137, wherein said nicotinic acid is dosed in the form of a sustained release tablet comprising from about 0.5 parts to about 2.5 parts by weight of a lubricating agent per 100 parts by weight of tablet.

(145) A method, as set forth in claim 144, wherein said lubricating agent is selected from the group consisting of stearic acid and magnesium stearate.

Group II claims - 146-202

(146) A daily method of treating hyperlipidemia in a patient comprising orally administering to the patient a sustained release composition of nicotinic acid once per day during the evening or as the patient lies down to go to sleep for providing an effective antihyperlipidemic amount of nicotinic acid to the patient during times of peak lipid production or synthesis by the patient to induce at least some lowering of total cholesterol, LDL cholesterol, triglycerides and Lp(a) and at least some increase in HDL cholesterol in the patient's blood stream, without causing abnormalities in uric acid levels or glucose levels or both to an extent which would require said daily treatment to be discontinued by the patient, the sustained release composition comprising an effective antihyperlipidemic amount of nicotinic acid and an excipient to provide sustained release of the nicotinic acid.

(147) A method of claim 146, wherein the effective antihyperlipidemic amount of nicotinic acid is from about 250 mg to about 3000 mg of nicotinic acid.

(148) A method of claim 146, wherein the excipient is selected from the group consisting of a swelling agent, a binder, a processing aid and mixtures thereof.

(149) A method of claim 148, wherein the swelling agent is selected from group consisting of a polymer, a wax, a natural material and mixtures thereof.

(150) A method of claim 149, wherein the polymer is selected from the group consisting of hydroxypropyl methylcellulose, sodium carboxymethylcellulose and ethylcellulose.

(151) A method of claim 149, wherein the wax is bees wax.

(152) A method of claim 149, wherein the natural material is selected from the group consisting of gums and gelatins.

(153) A method of claim 148, wherein the binder is povidone.

(154) A method of Claim 154, wherein the lubricant is stearic acid.

(155) A method of Claim 154, wherein the lubricant is stearic acid.

(156) A method of claim 150, wherein the hydroxypropyl methylcellulose is in an amount ranging from about 5% to about 50% parts by weight per 100 parts by weight of the sustained release composition.

(157) A method of claim 148, wherein the binder is in an amount ranging from about 1% to about 5% parts by weight per 100 parts by weight of the sustained release composition.

(158) A method of claim 148, wherein the processing aid is in an amount ranging from about 0.5% to about 2% parts by weight per 100 parts by weight of the sustained release composition.

(159) A method of claim 146, wherein the sustained release composition consists essentially of nicotinic acid, hydroxypropyl methylcellulose, povidone and stearic acid.

(160) A method of claim 146, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|---------------|
| nicotinic acid | 375.0 mg, |
| hydroxypropyl methylcellulose | 188.75 mg, |
| povidone | 12.9 mg., and |
| stearic acid | 5.8 mg. |

(161) A method of claim 146, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|-----------|
| nicotinic acid | 500.0 mg, |
| hydroxypropyl methylcellulose | 203.0 mg, |
| povidone | 17.2 and |
| stearic acid | 7.3 |

(162) A method of claim 146, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|----------|
| nicotinic acid | 750.0 |
| hydroxypropyl methylcellulose | 204.7 |
| povidone | 25.9 and |
| stearic acid | 9.9 |

(163) A sustained release composition of nicotinic acid for oral administration to a patient once per day during the evening or at night or as the patient lies down to go to sleep for providing and effective antihyperlipidemic amount of nicotinic acid to the patient during times of peak lipid production or synthesis by the patient to induce at least some lowering of total cholesterol, LDL cholesterol, triglycerides and Lp(a) and at least some increase in HDL cholesterol in the patient's blood stream, without causing abnormalities in uric acid levels or glucose levels or both to an extent which would require the use of said release composition by the patient to be discontinued, said sustained release composition comprising (a) an effective antihyperlipidemic amount of nicotinic acid, and (b) an excipient to provide sustained release of the nicotinic acid.

(164) A sustained release composition of claim 163, wherein said excipient is selected from the group consisting of a swelling agent, a binder, a processing aid and mixtures thereof.

(165) A sustained release composition of claim 164, wherein the swelling agent is selected from group consisting of a polymer, a wax, a natural material and mixtures thereof.

(166) A sustained release composition of claim 165, wherein the polymer is selected from the group consisting of hydroxypropyl methylcellulose, sodium carboxymethylcellulose and ethylcellulose.

(167) A sustained release composition of claim 165, wherein the wax is bees wax.

(168) A sustained release composition of claim 165, wherein the natural material is selected from the group consisting of gums and gelatins.

(169) A sustained release composition of claim 164, wherein the binder is povidone.

(170) A sustained release composition of claim 164, wherein the processing aid is a lubricant.

(171) A sustained release composition of claim 170, wherein the lubricant is stearic acid.

(172) A sustained release composition of claim 166, wherein the hydroxypropyl methylcellulose is in an amount ranging from about 5% to about 50% parts by weight per 100 parts by weight of the sustained release composition.

(173) A sustained release composition of claim 164, wherein the binder is in an amount ranging from about 1% to about 5% parts by weight per 100 parts by weight of the sustained release composition.

(174) A sustained release composition of claim 164, wherein the processing aid is in an amount ranging from about 0.5% to bout 2% parts by weight per 100 parts by weight of the sustained release composition.

(175) A sustained release composition of claim 163, wherein the sustained release composition consists essentially of nicotinic acid, hydroxypropyl methylcellulose, povidone and stearic acid.

(176) A sustained release composition of claim 163, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|---------------|
| nicotinic acid | 375.0 mg, |
| hydroxypropyl methylcellulose | 188.7 mg, |
| povidone | 12.9 mg., and |
| stearic acid | 5.8 mg. |

(178) A sustained release composition of claim 163, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|---------------|
| nicotinic acid | 500.0 mg, |
| hydroxypropyl methylcellulose | 203.0 mg, |
| povidone | 17.2 mg., and |
| stearic acid | 7.3 mg. |

(179) A sustained composition of claim 163, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|---------------|
| nicotinic acid | 750.0 mg, |
| hydroxypropyl methylcellulose | 204.7 mg, |
| povidone | 25.9 mg., and |
| stearic acid | 9.9 mg. |

(180) A daily method of treating hyperlipidemia in a patient without inducing treatment-limiting elevations in uric acid levels or glucose levels or both in the patient, said daily method comprising orally dosing the patient with an effective antihyperlipidemic amount of nicotinic acid once per day during the evening or at night or as the patient lies down to go to sleep as a single dose, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable carrier to form an oral sustained release solid dosage form.

(181) A method, as set forth in claim 180, wherein the patient is dosed with from about 250 mg to about 3000 mg of nicotinic acid.

(182) A method, as set forth in claim 181, wherein the release rate of the nicotinic acid is from about 2.0% per hour to about 25% per hour.

(183) A method, as set forth in claim 180, wherein the oral sustained release solid dosage form is prepared by formulating the nicotinic acid with from about 5 parts to about 50 parts by weight of hydroxypropyl methylcellulose per 100 parts by weight of the oral sustained release solid dosage form.

(184) A method, as set forth in claim 180, wherein the oral sustained release solid dosage form contains from about 1 part to about 4 parts by weight of binder per 100 parts by weight of the oral sustained release solid dosage form.

(185) A method, as set forth in claim 182, wherein the binder is a polymer having the repeating polymerization unit 1-ethenyl-2-pyrrolidone.

(186) A method, as set forth in claim 180, wherein the oral sustained release solid dosage form contains from about 0.5 parts to about 2.5 parts by weight of a lubricant per 100 parts by weight of the oral sustained release solid dosage form.

(187) A method, as set forth in claim 186, wherein the lubricant is selected from the group consisting of lubricants consisting of stearic acid and magnesium stearate.

(188) A method, as set forth in claim 180, wherein the oral sustained release solid dosage form contains from about 250 mg to about 3000 mg of nicotinic acid.

(189) A method, as set forth in claim 180, wherein the oral sustained release solid dosage form is an oral sustained release tablet.

(190) A method, as set forth in claim 189, wherein the oral sustained release tablet contains nicotinic acid in an amount selected from the group consisting of about 375 mg, about 500 mg and about 750 mg.

(191) A method, as set forth in claim 189, wherein the oral sustained release tablet contains

- (a) about 375 mg nicotinic acid,
- (b) about 189 mg hydroxypropyl methylcellulose as a swelling agent
- (c) about 13 mg a polymer having the repeating polymerization unit 1-ethenyl-2-pyrrolidone as a binder, and
- (d) about 6 mg of stearic acid as a lubricant.

(192) A method, as set forth in claim 189, wherein the oral sustained release tablet contains

- (a) about 500 mg nicotinic acid,
- (b) about 203 mg hydroxypropyl methylcellulose as a swelling agent
- (c) about 17.2 mg polyvinyl pyrrolidone as a binder, and
- (d) about 7.3 mg of stearic as a lubricant.

(193) A method, as set forth in claim 189, wherein the oral sustained release tablet contains

- (a) about 750 mg nicotinic acid,
- (b) about 205 mg hydroxypropyl methylcellulose as a swelling agent
- (c) about 26 mg polyvinyl pyrrolidone as a binder, and
- (d) about 10 mg of stearic as a lubricant.

(194) A method, as set forth in claim 189, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% by weight nicotinic acid,
- (b) about 5% to about 50% by weight hydroxypropyl methylcellulose as a swelling agent,
- (c) about 1% to about 5% by weight a polymer having repeating polymerization unit 1-ethenyl-2-pyrrolidone as a binder, and
- (d) about 0.5% to about 2% by weight stearic acid as a lubricant.

(195) A method, as set forth in claim 189, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% by weight nicotinic acid,
- (b) about 5% to about 50% by weight hydroxypropyl methylcellulose as a swelling agent.

(196) A method, as set forth in claim 180, wherein said single dose treatment during the evening or at night elevates HDL cholesterol in the patient.

(197) A daily method of treating hyperlipidemia in a patient without inducing treatment-limiting abnormalities in uric acid levels or glucose levels or both in the patient, said daily method comprising orally dosing the patient with an effective antihyperlipidemic amount of nicotinic acid once per day during the evening or at night or as the patient lies down to go to sleep as a single dose for providing an effective antihyperlipidemic amount of nicotinic acid to the patient during times of

peak lip production or synthesis by the patient to induce at least some decrease in levels of total cholesterol, LDL cholesterol, triglycerides and Lp(a) in the patient and to induce at least some increase in levels of HDL cholesterol in the patient, without causing abnormalities in either uric acid or glucose levels or both to an extent which would require said daily treatment to be discontinued by the patient, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form an oral sustained release solid dosage form.

(198) A method, as set forth in claim 197, wherein said single dose treatment induces at least some decrease in levels of total cholesterol, LDL cholesterol, triglycerides and Lp(a) in the patient.

(199) A method, as set forth in claim 197, wherein said single dose treatment elevates HDL cholesterol in the patient.

(200) A method of treating hyperlipidemia in a human without causing treatment-limiting elevations in uric acid levels or glucose levels or both in the human, said daily treatment comprising ingesting an oral sustained release nicotinic acid tablet once per day as a single dose for providing an effective antihyperlipidemic amount of nicotinic acid to the human during times of peak lipid production or synthesis by the human without causing treatment-limiting elevations in uric acid or glucose levels or both in the human, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form the oral sustained release tablet.

(201) A method, as set forth in claim 200, wherein said single dose treatment induces at least some decrease in levels of total cholesterol, LDL cholesterol, triglycerides and Lp(a) in the human.

(202) A method, as set forth in claim 200, wherein said single dose treatment elevates HDL cholesterol in the human.

Group III - claims 203-260

(203) A daily method of treating hyperlipidemia in a patient without inducing treatment-limiting liver damage, said daily method comprising orally dosing the patient with an effective antihyperlipidemic amount of nicotinic acid once per day during the evening or at night or as the patient lies down to go to sleep as a single dose, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable carrier to form an oral sustained release solid dosage form, said single daily dose treatment causing little or no serious damage to the liver of the patient.

(204) A method, as set forth in claim 203, wherein the patient is dosed with from about 250 mg to about 3000 mg of nicotinic acid.

(205) A method, as set forth in claim 204, wherein the release rate of the nicotinic acid is from about 2.0% per hour to about 25% per hour.

(206) A method, as set forth in claim 203, wherein the oral sustained release solid dosage form is prepared by formulating the nicotinic acid with from about 5 parts to about 50 parts by weight of hydroxypropyl methylcellulose per 100 parts by weight of the oral sustained release solid dosage form.

(207) A method, as set forth in claim 203, wherein the oral sustained release solid dosage form contains from about 1 part to about 4 parts by weight of binder per 100 parts by weight of the oral sustained release solid dosage form.

(208) A method, as set forth in claim 205, wherein the binder is a polymer having the repeating polymerization unit 1-ethenyl-2 pyrrolidone.

(209) A method, as set forth in claim 203, wherein the oral sustained release solid dosage form contains from about 0.5 parts to about 2.5 parts by weight of a lubricant per 100 parts by weight of the oral sustained release solid dosage form.

(210) A method, as set forth in claim 209, wherein the lubricant is selected from the group consisting of lubricants consisting of stearic acid and magnesium stearate.

(211) A method, as set forth in claim 203, wherein the oral sustained release solid dosage form contains from about 250 mg to about 3000 mg of nicotinic acid.

(212) A method, as set forth in claim 203, wherein the oral sustained release solid dosage form is an oral sustained release tablet.

(213) A method, as set forth in claim 212, wherein the oral sustained release tablet contains nicotinic acid in an amount selected from the group consisting of about 375 mg, about 500 mg and about 750 mg.

(214) A method, as set forth in claim 212, wherein the oral sustained release tablet contains

- (a) about 375 mg nicotinic acid,
- (b) about 189 mg hydroxypropyl methylcellulose as a swelling agent
- (c) about 13 mg a polymer having the repeating polymerization unit 1-ethenyl-2-pyrrolidone as a binder, and
- (d) about 6 mg of stearic as a lubricant.

(215) A method, as set forth in claim 212, wherein the oral sustained release tablet contains

- (a) about 500 mg nicotinic acid,
- (b) about 203 mg hydroxypropyl methylcellulose as a swelling agent
- (c) about 17.2 mg polyvinyl pyrrolidone as a binder, and
- (d) about 7.3 mg of stearic acid as a lubricant.

(216) A method, as set forth in claim 212, wherein the oral sustained release tablet contains

- (a) about 750 mg nicotinic acid,
- (b) about 205 mg hydroxypropyl methylcellulose as a swelling agent
- (c) about 26 mg polyvinyl pyrrolidone as a binder, and
- (d) about 10 mg of stearic acid as a lubricant.

(217) A method, as set forth in claim 212, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% by weight nicotinic acid,
- (b) about 5% to about 50% by weight hydroxypropyl methylcellulose as a swelling agent,
- (c) about 1% to about 5% by weight a polymer having repeating polymerization unit 1-ethenyl-2-pyrrolidone as a binder, and
- (d) about 0.5% to about 2% by weight stearic acid as a lubricant.

(218) A method, as set forth in claim 212, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% by weight nicotinic acid,
- (b) about 5% to about 50% parts by weight hydroxypropyl methylcellulose as a swelling agent.

(219) A method, as set forth in claim 203, wherein said single dose treatment during the evening or at night elevates HDL cholesterol in the patient.

(220) A method, as set forth in claim 203, wherein said single dose treatment during the evening or at night results in little or no serious increase in a liver function test in the patient, wherein the liver function test is selected from the group consisting of an AST, ALT and alkaline phosphatase liver function test.

(221) A method, as set forth in claim 203, wherein said single dose treatment during the evening or at night results in little or no serious increase in uric acid in the patient.

(222) A method, as set forth in claim 203, wherein said single dose treatment during the evening or at night results in little or no serious increase in free fasting glucose in the patient.

(223) A daily method of treating hyperlipidemia in a patient without inducing treatment-limiting hepatotoxicity, said daily method comprising orally dosing the patient with an effective amount of nicotinic acid once per day during the evening or at night or as the patient lies down to go to sleep as a single dose for reducing hyperlipidemia in the patient, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form an oral sustained release

solid dosage form, and wherein said single daily nicotinic acid dose treatment administered during the evening or at night is at least as effective in lowering at least one serum lipid in a patient wherein the serum lipid is selected from the group consisting of total cholesterol, LDL cholesterol, triglycerides and Lp(a), as treatment with an oral sustained release nicotinic acid preparation when it is dosed daily in two divided doses at a total daily nicotinic acid dosage which is at least equivalent to said single daily nicotinic acid dose treatment administered only during the evening or at night, and wherein said single daily nicotinic acid dose treatment administered during the evening or at night is essentially free of treatment-limiting hepatotoxic side effects which are generally associated with the oral sustained release nicotinic acid preparation when it is dosed daily in two divided doses at a total daily nicotinic acid dosage which is at least equivalent to said single daily nicotinic acid dose treatment administered during the evening or at night.

(224) A method, as set forth in claim 223, wherein the patient is dosed with from 250 mg to about 3000 mg of nicotinic acid.

(225) A method, as set forth in claim 223, wherein the release rate of said nicotinic acid is from about 2.0% per hour to about 25% per hour.

(226) A method, as set forth in claim 223, wherein the oral solid dosage form is prepared by formulating the nicotinic acid with from about 5 to about 50 parts by weight of hydroxypropyl methylcellulose per 100 parts by weight of the oral solid dosage form.

(227) A method, as set forth in claim 223, wherein the oral solid dosage form further contains from about 1 to about 4 parts by weight of a binder per 100 parts by weight of the oral solid dosage form.

(228) A method, as set forth in claim 227, wherein the binder is polyvinyl pyrrolidone.

(229) A method, as set forth in claim 223, wherein the oral solid dosage form further contains from about 0.5 to about 2.5 parts by weight of a lubricant per 100 parts by weight of the oral solid dosage form.

(230) A method, as set forth in claim 229, wherein the lubricant is selected from the group consisting of stearic acid and magnesium stearate.

(231) A method, as set forth in claim 223, wherein the oral sustained release solid dosage form contains from about 250 mg to about 3000 mg of nicotinic acid.

(232) A method, as set forth in claim 223, wherein the oral sustained release solid dosage form is an oral sustained release tablet.

(233) A method, as set forth in claim 232, wherein the oral sustained released tablet contains nicotinic acid in an amount selected from the group consisting of about 375 mg, about 500 mg and about 750 mg.

(234) A method, as set forth in claim 232, wherein the oral sustained release tablet contains

- (a) about 375 mg nicotinic acid,
- (b) about 189 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 13 mg polyvinyl pyrrolidone as a binder, and
- (d) about 6 mg of stearic acid as a lubricant.

(235) A method, as set forth in claim 232, wherein the oral sustained release tablet contains

- (a) about 500 mg nicotinic acid,
- (b) about 203 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 17 mg polyvinyl pyrrolidone as a binder, and
- (d) about 7 mg of stearic acid as a lubricant.

(236) A method, as set forth in claim 232, wherein the oral sustained release tablet contains

- (a) about 750 mg nicotinic acid,
- (b) about 205 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 26 mg polyvinyl pyrrolidone as a binder, and
- (d) about 10 mg stearic acid as a lubricant.

(237) A method, as set forth in claim 232, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% by weight nicotinic acid,
- (b) about 5% to about 50% by weight hydroxypropyl methylcellulose as a swelling agent,
- (c) about 1% to about 5% by weight polyvinyl pyrrolidone as a binder, and
- (d) about 0.5% to about 2% by weight stearic acid as a lubricant.

(238) A method, as set forth in claim 232, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% parts by weight nicotinic acid, and
- (b) about 5% to about 50% parts by weight hydroxypropyl methylcellulose as a swelling agent.

(239) A method, as set forth in claim 223, wherein said single dose treatment during the evening or at night elevates HDL cholesterol in the patient.

(240) A method, as set forth in claim 223, wherein said single dose treatment during the evening or at night results in little or no serious increase in a liver function test in the patient, wherein the liver function test is selected from the group consisting of an AST, ALT and alkaline phosphatase liver function test.

(241) A method, as set forth in claim 223, wherein said single dose treatment during the evening or at night results in little or no serious increase in uric acid in the patient.

(242) A method, as set forth in claim 223, wherein said single dose treatment during the evening or at night results in little or no serious increase in free fasting glucose in the patient.

(243) A method of treating hyperlipidemia in a patient comprising orally dosing the patient with an effective amount of nicotinic acid once per day during the evening or at night or as the patient lies down to go to sleep as a single dose for lowering serum lipids, wherein said single nicotinic acid dosing is accomplished by ingestion of an oral sustained release tablet comprising nicotinic acid, a swelling agent, a binder and a lubricant, wherein said single nicotinic acid dosing during the evening or at night is at least as effective in lowering at least one serum lipid in a patient,

wherein the serum lipid is selected from the group consisting of total cholesterol, LDL cholesterol, triglycerides and Lp(a), as treatment with an oral sustained release nicotinic acid preparation when it is dosed in two daily divided doses at a total daily nicotinic acid dosage which is at least equivalent to said single nicotinic acid dose treatment administered during the evening or at night, and wherein said single nicotinic acid dosing administered during the evening or at night causes less elevations in liver function tests than treatment with the oral sustained release nicotinic acid preparation when it is dosed in two daily divided doses at a total daily nicotinic acid dosage which is at least equivalent to said single nicotinic acid dosing administered during the evening or at night.

(244) A method, as set forth in claim 243, wherein the patient is dosed with from 250 mg to about 3000 mg of nicotinic acid.

(245) A method, as set forth in claim 243, wherein the release rate of said nicotinic acid is from about 2.0% per hour to about 25% per hour.

(246) A method, as set forth in claim 243, wherein said single dose treatment during the evening or at night elevates HDL cholesterol in the patient.

(247) A method, as set forth in claim 243, wherein said single dose treatment during the evening or at night results in little or no serious increase in a liver function test in a patient wherein the liver function test is selected from the group consisting of an AST, ALT and alkaline phosphatase liver function test.

(248) A method, as set forth in claim 243, wherein said single dose treatment during the evening or at night results in little or no serious increase in uric acid in the patient.

(249) A method, as set forth in claim 243, wherein said single dose treatment during the evening or at night results in little or no serious increase in free fasting glucose in the patient.

(250) A method, as set forth in claim 243, wherein the oral sustained release tablet contains about 5 to about 50 parts by weight of hydroxypropyl methylcellulose per 100 parts by weight of the oral sustained release tablet as the swelling agent.

(251) A method, as set forth in claim 243, wherein the oral sustained release tablet further contains about 1 to about 4 parts by weight of a binder per 100 parts by weight of the oral sustained release tablet.

(252) A method, as set forth in claim 251, wherein the binder is polyvinyl pyrrolidone.

(253) A method, as set forth in claim 243, wherein the oral sustained release tablet further contains about 0.5 to about 2.5 parts by weight of a lubricant per 100 parts by weight of the oral sustained release tablet.

(254) A method, as set forth in claim 253, wherein the lubricant is selected from the group consisting of stearic acid and magnesium stearate.

(255) A method, as set forth in claim 243, wherein the oral sustained release tablet contains from about 250 mg to about 3000 mg of nicotinic acid.

(256) A method, as set forth in claim 243, wherein the sustained release tablet contains

- (a) about 30% to about 90% parts by weight nicotinic acid,
- (b) about 5% to about 50% parts by weight hydroxypropyl methylcellulose as the swelling agent.

(257) A method, as set forth in claim 243, wherein the oral sustained release tablet contains

- (a) about 30% to about 90% by weight nicotinic acid,
- (b) about 5% to about 50% by weight hydroxypropyl methylcellulose as a swelling agent,
- (c) about 1% to about 5% by weight a polymer having repeating polymerization unit 1-ethenyl-2-pyrrolidone as a binder, and
- (d) about 0.5% to about 2% by weight stearic acid as a lubricant.

(258) A method, as set forth in claim 243, wherein the sustained release tablet contains

- (a) about 375 mg nicotinic acid,
- (b) about 189 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 13 mg polyvinyl pyrrolidone as a binder, and
- (d) about 6 mg of stearic acid as a lubricant.

(259) A method, as set forth in claim 243, wherein the sustained release tablet contains

- (a) about 500 mg nicotinic acid,
- (b) about 203 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 17 mg polyvinyl pyrrolidone as a binder, and
- (d) about 7 mg of stearic acid as a lubricant.

(260) A method, as set forth in claim 243, wherein the sustained release tablet contains

- (a) about 750 mg nicotinic acid,
- (b) about 205 mg hydroxypropyl methylcellulose as a swelling agent,
- (c) about 26 mg polyvinyl pyrrolidone as a binder, and
- (d) about 10 mg stearic acid as a lubricant.

Group IV - claims 261-294

(261) A method of treating hyperlipidemia in a patient without inducing treatment-limiting (i) hepatotoxicity and (ii) abnormalities in uric acid levels or glucose levels or both, said method comprising orally dosing the patient with an effective antihyperlipidemic amount of nicotinic acid once per day during the evening or at night or as the patient lies down to go to sleep as a single dose, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form an oral sustained release solid dosage form, wherein the oral sustained release solid dosage form is effective in reducing a serum lipid without causing treatment-limiting (i) hepatotoxicity and (ii) elevations in uric acid levels or glucose levels or both in the patient to a level which would require said treatment to be discontinued by the patient when it is ingested by the patient once per day during the evening or at night as the single dose in accordance with said single dose treatment.

(262) A daily method of treating hyperlipidemia in a patient comprising orally administering to the patient a sustained release composition of nicotinic acid once per day during the evening or or night or as the patient lies down to go to sleep for providing an effective antihyperlipidemic amount of nicotinic acid to the patient during times of peak lipid production or synthesis by the patient to induce at least some lowering of total cholesterol, LDL cholesterol, triglycerides and Lp(a) and at least some increase in HDL cholesterol in the patient's blood stream, without causing abnormalities in liver function tests and uric acid levels or glucose levels to an extent which would require said daily treatment to be discontinued by the patient, the sustained release composition comprising an effective antihyperlipidemic amount of nicotinic acid and an excipient to provide sustained release of the nicotinic acid.

(263) A method of claim 262, wherein the effective antihyperlipidemic amount of nicotinic acid is from about 250 mg to about 3000 mg of nicotinic acid.

(264) A method of claim 262, wherein the excipient is selected from the group consisting of a swelling agent, a binder, a processing aid and mixtures thereof.

(265) A method of claim 264, wherein the swelling agent is selected from group consisting of a polymer, a wax, a natural material and mixtures thereof.

(266) A method of claim 265, wherein the polymer is selected from the group consisting of hydroxypropyl methylcellulose, sodium carboxymethylcellulose and ethylcellulose.

(267) A method of claim 265, wherein the wax is bees wax.

(268) A method of claim 265, wherein the natural material is selected from the group consisting of gums and gelatins.

(269) A method of claim 264, wherein the binder is povidone.

(270) A method of claim 264, wherein the processing aid is a lubricant.

(271) A method of Claim 270, wherein the lubricant is stearic acid.

(272) A method of claim 266, wherein the hydroxypropyl methylcellulose is in an amount ranging from about 5% to about 50% parts by weight per 100 parts by weight of the sustained release composition.

(273) A method of claim 264, wherein the binder is in an amount ranging from about 1% to about 5% parts by weight per 100 parts by weight of the sustained release composition.

(274) A method of claim 264, wherein the processing aid is in an amount ranging from about 0.5% to about 2% parts by weight per 100 parts by weight of the sustained release composition.

(275) A method of claim 262, wherein the sustained release composition consists essentially of nicotinic acid, hydroxypropyl methylcellulose, povidone and stearic acid.

(276) A method of claim 262, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|---------------|
| nicotinic acid | 375.0 mg, |
| hydroxypropyl methylcellulose | 188.7 mg, |
| povidone | 12.9 mg., and |
| stearic acid | 5.8 mg. |

(277) A method of claim 262, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 500.0 mg, |
| hydroxypropyl methylcellulose | 203.0 mg, |
| povidone | 17.2 mg, and |
| stearic acid | 7.3 mg |

(278) A method of claim 262, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 750.0 mg. |
| hydroxypropyl methylcellulose | 204.7 mg. |
| povidone | 25.9 mg. and |
| stearic acid | 9.9 mg. |

(279) A sustained release composition of nicotinic acid for oral administration to a patient once per day during the evening or night or as the patient lies down to go to sleep for providing an effective antihyperlipidemic amount of nicotinic acid to the patient during times of peak lipid production or synthesis by the patient to induce at least some lowering of total cholesterol, LDL cholesterol, triglycerides and Lp(a) and at least some increase in HDL cholesterol in the patient's blood stream, without causing abnormalities in liver function tests and uric acid levels or glucose levels or both to an extent which would require the use of said sustained release composition by the patient to be discontinued, the sustained release composition comprising (a) an effective antihyperlipidemic amount of nicotinic acid, and (b) an excipient to provide sustained release of the nicotinic acid.

(280) A sustained release composition of claim 279, wherein said excipient is selected from the group consisting of a swelling agent, a binder, a processing aid and mixtures thereof.

(281) A sustained release composition of claim 280, wherein the swelling agent is selected from group consisting of a polymer, a wax, a natural material and mixtures thereof.

(282) A sustained release composition of claim 281, wherein the polymer is selected from the group consisting of hydroxypropyl methylcellulose, sodium carboxymethylcellulose and ethylcellulose.

(283) A sustained release composition of claim 281, wherein the wax is bees wax.

(284) A sustained release composition of claim 281, wherein the natural material is selected from the group consisting of gums and gelatins.

(285) A sustained release composition of claim 280, wherein the binder is povidone.

(286) A sustained release composition of claim 280, wherein the processing aid is a lubricant.

(287) A sustained release composition of claim 286, wherein the lubricant is stearic acid.

(288) A sustained release composition of claim 282, wherein the hydroxypropyl methylcellulose is in an amount ranging from about 5% to about 50% parts by weight per 100 parts by weight of the sustained release composition.

(289) A sustained release composition of claim 280, wherein the binder is in an amount ranging from about 1% to about 5% parts by weight per 100 parts by weight of the sustained release composition.

(290) A sustained release composition of claim 280, wherein the processing aid is in an amount ranging from about 0.5% to about 2% parts by weight per 100 parts by weight of the sustained release composition.

(291) A sustained release composition of claim 279, wherein the sustained release composition consists essentially of nicotinic acid, hydroxypropyl methylcellulose, povidone and stearic acid.

(292) A sustained release composition of claim 279, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 375.0 mg. |
| hydroxypropyl methylcellulose | 188.7 mg. |
| povidone | 12.9 mg. and |
| stearic acid | 5.8 mg. |

(293) A sustained release composition of claim 279, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 500.0 mg. |
| hydroxypropyl methylcellulose | 203.0 mg. |
| povidone | 17.2 mg. and |
| stearic acid | 7.3 mg. |

(294) A sustained release composition of claim 279, wherein the sustained release composition consists essentially of

| | |
|-------------------------------|--------------|
| nicotinic acid | 750.0 mg. |
| hydroxypropyl methylcellulose | 204.7 mg. |
| povidone | 25.9 mg. and |
| stearic acid | 9.9 mg. |